

## Genetic Drift

### The Good That We Do

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One day, I was on the ward, teaching the pediatric house staff how to do an examination for findings that should prompt a genetic consultation. "None," said a third-year medical student, smiling as if he'd made a most clever observation. "What good do you do? Maybe you can make an obscure diagnosis, give us something to call 'it'. But you can't fix it."

I'd be lying if I said I didn't ask myself that same question from time to time, usually after another long session of explaining to parents that their child has a terrible condition that we can do little about. At times I feel as if I should find my stethoscope and otoscope (I'd have to recharge the battery), learn about all the new antibiotics, and practice general pediatrics. However, when this happens, I remember Jessica.

Jessica was hard to track down, but I needed her, so I persisted. She was a member of a family with cleidocranial dysplasia, a key family in the genetic linkage study in which I was involved at the time. Most of this family was wonderfully cooperative. Weeks before, they had invited me to a family reunion for examinations and blood drawing on the family. "It's no bother—we have a reunion about every other week," they told me. But that day I noted that some of the people listed in the pedigree were missing.

"I don't know where Barry's family is," said Andy, the oldest child, the one who'd organized the reunion. "And Ray, he's out west, I think. We don't hear from him. But his daughter lives downtown."

"He had children?," I asked, looking at the pedigree.

"Yes sir. Jessie. She lives with her mother. She must be 18 by now."

"Her mother works at the warehouse. I see her now and again, around town. I'll get in touch with her and tell her to give you a call, but I don't know if she will."

I left my number with little hope or expectation. To my surprise, Mrs. Askins called the next day. "Dr. Robin? I'm Sheila Askins. First, tell me. Does this have anything to do with Ray?"

"Well, yes in a way it does," I said, and added quickly, "but it really has more to do with your daughter." I went on to explain the study and described it as research on genetic problems of the teeth, problems like those was seen in her ex-husband and his relatives.

Almost immediately, she interrupted. "My daughter has the same bad teeth, just like Ray and his brothers. Her teeth are awful. She's in the oral surgeon's office twice a month. And she's got these other problems, with her back, and her shoulder. My poor girl, she has so much wrong, she spends more time at the doctor than her 82-year-old grandmother. I don't know why she has so much wrong with her. . . ." Her voice trailed off into a sob.

"Mrs. Askins, would you be willing to come with your daughter to the hospital?," I said. "We can talk more about your daughter's problems, and if you and she are willing to participate in the study, we can draw the blood samples for the study." She agreed readily, saying she'd bring her daughter in later that week.

I was worried that Mrs. Askins and Jessica might not keep the appointment, but they came in early. They were both reserved: their eyes would not meet mine when I introduced myself. After the preliminary questions and comments, I asked Jessica to tell me about her medical problems.

"Oh, you don't have that much time, doctor," she said with a sad smile.

Jessica had a very delicate facial structure, very different from the prominent forehead and maxillary underdevelopment usually seen in those with cleidocranial dysplasia. In this respect, she resembled her mother, a tall, thin woman in her 50s. The only obvious sign that Jessica was affected was in her smile, which exposed a mouth full of wires and metal bands.

She told me about the six different operations that she'd had to remove her extra teeth and realign the remaining ones and about the braces she'd worn since age 7. "They're coming off later this year, or maybe the next," her mother said. "That's what Dr. Gordon said last year, too, mother," Jessie added, clearly not allowing herself any optimism. "But I have other problems, too."

Her back hurt. She had a curvature of the spine because of a defective bone in her back. It hurt if she stood or walked for a long time. She needed a special mattress, but it didn't really help. Her hips hurt. The doctor said she had early arthritis; she used to take Advil®, but it had stopped being effective last summer.

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Essays in "Genetic Drift" emphasize the human side of genetics. Where appropriate, names and locations are changed to maintain confidentiality.

Now, she had a prescription drug but was afraid to take it: "I don't want to get hooked on drugs."

"I used to play tennis, back in junior high, but one day my shoulder began to hurt. I went to the doctor, and he said I was missing some bones in my shoulder, my collar bones. He said there was nothing he could do, it was something that I had to live with. But what does this all have to do with my teeth problem that you're doing this research on?"

It was then that I began to explain to her about cleidocranial dysplasia, how all of her problems were caused by a single gene that had become nonfunctional. There was no way to influence what it did, or how it was passed on. We were trying to find where the gene was located on the chromosomes so that in the future we might be able to treat it more effectively. I said that I'd need to examine Jessica, so I handed her a gown and told her I'd be back in a few minutes.

I stepped out of the room and paused. I was stunned. Had no one thought that all of these problems might be related? This poor girl had been shuffled from one doctor to another, and no one had recognized the big picture.

After a few minutes, I announced myself with a knock on the examining-room door. I heard only a muffled sound in reply. Entering, I saw Jessica sobbing in her mother's arms. Her mother was crying as well. Oh my God, I thought, what did I do? Did I need to cause the two of them to suffer any more? "I'm sorry if anything I said upset you," I said, "I really didn't mean to."

Jessica's mother looked up at me, her eyes now red from crying. "Doctor, my girl has been through hell.

And the worst of it has been, well . . . , we just couldn't understand it. Why did God put this on her? Why she had so much wrong with her, her back, her hips, her shoulders, and her teeth . . . ?" She was sobbing uncontrollably now, so badly that Jessica began to comfort her mother.

"It's all because of one problem?" Jessica asked, "one gene that doesn't work right? All of this, the teeth, the back. It's all from one thing?"

"Yes," I said, "all of your problems, the teeth, the back, the hips, and your shoulders. They're all caused by a single, changed gene."

Jessica smiled, shaking her head in apparent disbelief, with a look of relief on her face.

By using the blood samples obtained from that family, our lab went on to make important discoveries, and we published some fine scientific papers. But that is not what I remember most from that work or what I am most proud of. Rather, it is that afternoon I spent with Jessica and her mother. They left that day with a new outlook on their lives: Jessica was freed from the burden of "being cursed" with a host of medical ailments, and her mother was relieved from the guilt that she had caused her daughter's problems.

I did not cure or fix any of Jessica's physical ailments, but I did give her and her mother something else that day: information, which gave them some peace of mind. I looked at that medical student and thought of Jessica and her mother. I smiled and shook my head. "What good do geneticists do? A little bit here, a bit there, and sometimes a whole lot. It adds up."